ERCC8 gene

ERCC excision repair 8, CSA ubiquitin ligase complex subunit

Normal Function

The *ERCC8* gene provides instructions for making a protein called Cockayne syndrome A (CSA), which is involved in repairing damaged DNA. DNA can be damaged by ultraviolet (UV) rays from the sun and by toxic chemicals, radiation, and unstable molecules called free radicals. The damage caused by these agents can block vital cell activities such as gene transcription, which is the first step in protein production. If left uncorrected, DNA damage accumulates, which causes cells to malfunction and can lead to cell death.

Although DNA damage occurs frequently, cells are usually able to fix it before it can cause problems. Cells have several mechanisms to correct DNA damage; one such mechanism involves the CSA protein. This protein specializes in repairing damaged DNA within active genes (those genes undergoing gene transcription). However, its specific role in this process is unclear. The CSA protein interacts with other proteins, probably to identify areas of damaged DNA.

Health Conditions Related to Genetic Changes

Cockayne syndrome

Researchers have identified more than 30 *ERCC8* gene mutations that can cause Cockayne syndrome. This rare condition includes a variety of features, including an abnormally small head size (microcephaly), very slow growth resulting in short stature, delayed development, and an increased sensitivity to sunlight (photosensitivity).

Some of the *ERCC8* gene mutations result in the production of an abnormally short version of the CSA protein that cannot function properly. Other mutations change one of the building blocks (amino acids) used to make the CSA protein, which also results in a malfunctioning protein.

The mechanism by which *ERCC8* gene mutations lead to Cockayne syndrome is not well understood. The altered CSA protein probably disrupts DNA repair. As a result, damaged DNA is not fixed, which disrupts gene transcription and prevents the normal production of proteins. These abnormalities impair cell function and eventually lead to the death of cells in many organs and tissues. Faulty DNA repair underlies photosensitivity in affected individuals, and researchers suspect that it also contributes to the other features of Cockayne syndrome. It is unclear how *ERCC8* gene mutations cause all of the varied features of this condition.

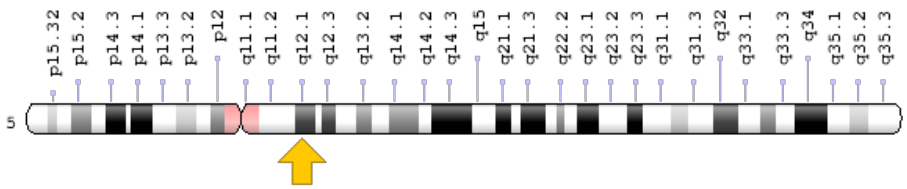
UV-sensitive syndrome

At least one mutation in the *ERCC8* gene can cause UV-sensitive syndrome, a condition characterized by unusual sensitivity to UV rays from the sun. People with UV-sensitive syndrome sunburn easily and have freckled skin or other changes in skin coloring (pigmentation). The known mutation replaces the amino acid tryptophan with the amino acid cysteine at position 361 in the CSA protein (written as Trp361Cys or W361C). Although the effect of this change on the function of the protein is unknown, it somehow prevents cells from repairing DNA damage caused by UV rays, and transcription of damaged genes is blocked. It is unclear exactly how an abnormal CSA protein causes the signs and symptoms of UV-sensitive syndrome. Additionally, it is unknown why the Trp361Cys mutation causes photosensitivity without the other features of Cockayne syndrome (described above).

Chromosomal Location

Cytogenetic Location: 5q12.1, which is the long (q) arm of chromosome 5 at position 12.1

Molecular Location: base pairs 60,873,832 to 60,945,078 on chromosome 5 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- CKN1
- Cockayne syndrome 1 (classical)
- Cockayne syndrome 1 protein
- Cockayne syndrome, type A
- CSA
- ERCC8_HUMAN
- excision repair cross-complementation group 8
- excision repair cross-complementing rodent repair deficiency, complementation group 8

Additional Information & Resources

Educational Resources

- Molecular Biology of the Cell (fourth edition, 2002): DNA Repair
  https://www.ncbi.nlm.nih.gov/books/NBK26879/

GeneReviews

- Cockayne Syndrome
  https://www.ncbi.nlm.nih.gov/books/NBK1342

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28ERCC8%5BTIAB%5D%29+OR+%28CKN1%5BTIAB%5D%29%29+OR+%28%28CSA%5BTI%5D%29+AND+%28Cockayne%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D

OMIM

- EXCISION REPAIR CROSS-COMPLEMENTING, GROUP 8
  http://omim.org/entry/609412

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/CSAID301.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=ERCC8%5Bgene%5D
- HGNC Gene Family: ERCC excision repair associated
  http://www.genenames.org/cgi-bin/genefamilies/set/1268
- HGNC Gene Family: WD repeat domain containing
  http://www.genenames.org/cgi-bin/genefamilies/set/362
- HGNC Gene Symbol Report
  http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=3439
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/1161
- UniProt
  http://www.uniprot.org/uniprot/Q13216

Sources for This Summary

- Bertola DR, Cao H, Albano LM, Oliveira DP, Kok F, Marques-Dias MJ, Kim CA, Hegele RA. Cockayne syndrome type A: novel mutations in eight typical patients. J Hum Genet. 2006;51(8): 701-5. Epub 2006 Jul 25.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16865293
- Cao H, Williams C, Carter M, Hegele RA. CKN1 (MIM 216400): mutations in Cockayne syndrome type A and a new common polymorphism. J Hum Genet. 2004;49(1):61-3. Epub 2003 Dec 6.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/14661080
- Kamiuchi S, Saijo M, Citterio E, de Jager M, Hoeijmakers JH, Tanaka K. Translocation of Cockayne syndrome group A protein to the nuclear matrix: possible relevance to transcription-coupled DNA repair. Proc Natl Acad Sci U S A. 2002 Jan 8;99(1):201-6.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/11782547
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC117539/
- Laugel V, Dalloz C, Durand M, Sauvanaud F, Kristensen U, Vincent MC, Pasquier L, Odent S, Cormier-Daire V, Gener B, Tobias ES, Tolmie JL, Martin-Coignard D, Drouin-Garraud V, Heron D, Journel H, Raffo E, Vigneron J, Lyonnet S, Murday V, Gubser-Mercati D, Funalot B, Brueton L, Sanchez Del Pozo J, Muñoz E, Gennery AR, Salih M, Noruzinia M, Prescott K, Ramos L, Stark Z, Fieggen K, Chabrol B, Sarda P, Edery P, Bloch-Zupan A, Fawcett H, Pham D, Egly JM, Lehmann AR, Sarasin A, Dollfus H. Mutation update for the CSB/ERCC6 and CSA/ERCC8 genes involved in Cockayne syndrome. Hum Mutat. 2010 Feb;31(2):113-26. doi: 10.1002/humu.21154.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/19894250
- Laugel V. Cockayne syndrome: the expanding clinical and mutational spectrum. Mech Ageing Dev. 2013 May-Jun;134(5-6):161-70. doi: 10.1016/j.mad.2013.02.006. Epub 2013 Feb 18. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/23428416
- Nardo T, Oneda R, Spivak G, Vaz B, Mortier L, Thomas P, Orioli D, Laugel V, Stary A, Hanawalt PC, Sarasin A, Stefanini M. A UV-sensitive syndrome patient with a specific CSA mutation reveals separable roles for CSA in response to UV and oxidative DNA damage. Proc Natl Acad Sci U S A. 2009 Apr 14;106(15):6209-14. doi: 10.1073/pnas.0902113106. Epub 2009 Mar 27.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/19329487
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2667150/
- Saijo M. The role of Cockayne syndrome group A (CSA) protein in transcription-coupled nucleotide excision repair. Mech Ageing Dev. 2013 May-Jun;134(5-6):196-201. doi: 10.1016/j.mad.2013.03.008. Epub 2013 Apr 6. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/23571135
- Spivak G, Hanawalt PC. Host cell reactivation of plasmids containing oxidative DNA lesions is defective in Cockayne syndrome but normal in UV-sensitive syndrome fibroblasts. DNA Repair (Amst). 2006 Jan 5;5(1):13-22. Epub 2005 Aug 29.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16129663

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